IN THE CLAIMS:

Please amend claims 1, 5, 20-22, 26-28, 34, 37, 38 and 40 and cancel claims 41-44.

This listing of claims will replace all prior versions, and listings of the claims in the application.

Listing of the claims

1. (Currently Amended) A method of identifying an alternatively spliced RNA molecule in conjunction with a normally spliced counterpart RNA molecule, comprising the steps of:

~~(1)~~(a) obtaining a first population of cDNA molecules from a biological sample representing a first physiological condition and a second population of cDNA molecules from a biological sample representing a second physiological condition;

~~(2)~~(b) attaching a first selectable tag to cDNA molecules of the first cDNA population and a second selectable tag to cDNA molecules of the second cDNA population, wherein the first and second selectable tags are different;

~~(3)~~(c) combining, denaturing and annealing cDNA molecules from both the first and second cDNA populations, to obtain a mixed population of cDNA molecules including cross-hybridized double-stranded cDNA that comprises both a single strand that is from the first population of cDNA and that is attached to the first selectable tag, and a single strand that is from the second population of cDNA and that is attached to the second selectable tag;

~~(4)~~(d) isolating cross-hybridized double-stranded cDNA that comprises both the first and second selectable tags from the mixed population~~, wherein the double-stranded cDNA comprises the first and second selectable tags, and also comprises a cDNA molecule from the first cDNA population and a cDNA molecule from the second cDNA population~~;

~~(5)~~(e) selecting from the cross-hybridized double-stranded cDNA isolated in step ~~(4)~~(d), cross-hybridized double-stranded cDNA which comprises at least one ~~region~~ area of mismatched sequence present as an unhybridized single-stranded nucleic acid;

~~(6)~~(f) coupling at one end the cross-hybridized double stranded cDNA, both strands of ~~each~~ the cross-hybridized double-stranded cDNA ~~from~~ selected in step ~~(5)~~(e) to each other by linking the 3' end of one strand to the 5' end of the other strand to obtain a coupled double-stranded cDNA molecule that comprises at least one area of mismatched sequence, wherein when denatured said coupled double-stranded cDNA is a linear single stranded nucleic acid molecule;

(g) denaturing the coupled double-stranded cDNA to form a linear single stranded nucleic acid molecule; and

~~(7)~~(h) analyzing ~~comparing both strands of the coupled molecule, wherein one strand of the coupled molecule represents~~ the sequence of the linear single stranded nucleic acid molecule derived from the cross-hybridized double stranded cDNA to identify the sequence of an alternatively spliced RNA molecule~~, and the other strand represents the normally spliced~~

~~counterpart RNA molecule~~ through comparison of the region of the sequence derived from the first population of cDNA to the region of the sequence derived from the second population of cDNA.

2. (Previously Presented) The method of claim 1, wherein the first biological sample comprises normal tissue, and the second biological samples comprises diseased tissue.

3. (Previously Presented) The method of claim 1, wherein the first and second biological samples comprise tissue in different developmental states.

4. (Previously Presented) The method of claim 1, wherein the first biological sample comprises untreated tissue, and the second biological sample comprises tissue which has been treated with a therapeutic or toxic agent.

5. (Currently Amended) The method of claim 1, wherein first and second biological samples ~~can also~~ comprise tissue or cells from different species.

6. (Previously Presented) The method of claim 1, wherein the first and second biological samples are derived from a human.

7. (Previously Presented) The method of claim 2, wherein the second biological sample comprises tumor or neoplastic tissue.

8. (Previously Presented) The method of claim 7, wherein the tumor or neoplastic tissue is derived from a subject with acute promyelocytic leukemia; acute lymphoblastic leukemia; myeloblastic leukemia; uterine cancer; thyroid cancer; gastrointestinal tumors; dysplastic and neoplastic cervical epithelium; melanoma; breast cancer; prostate cancer; lung cancer; endometrial cancer; teratocarcinoma; colon cancer; brain and desmoplastic round cell tumors; epithelial neoplasias; gastric cancer; ovarian cancer or sarcomas, myomas, myxomas, ependymomas, fibromas, neurofibrosarcomas.

9. (Previously Presented) The method of claim 2, wherein the second biological sample comprises diseased tissue derived from a subject with infection, stress, disorders or conditions of the immune system; a metabolic disorder; a collagen disorder; a psychiatric disorder, a skin disorder, a liver disorder, a disorders of the arteries; an inherited red cell membrane disorder; thyroid hormone repression; endometrial hyperplasia; Alzheimer's disease; or alcoholism.

10. (Previously Presented) The method of claim 1, wherein the first and second cDNA populations are synthesized from RNA populations which have been enriched for polyA+ RNA.

11. (Previously Presented) The method of claim 1, wherein at least one cDNA population comprises double-stranded cDNA.

12. (Previously Presented) The method of claim 1, wherein the first and second cDNA populations comprise double-stranded cDNA.

13. (Previously Presented) The method of claim 1, wherein the first and second selectable tags are selected from the group consisting of: biotin; avidin; streptavidin; antigens; haptens; antibodies; hormones; vitamins; receptors; carbohydrates; lectins; metals; chelators; polynucleotides; cofactor or prosthetic groups; apoproteins; effector molecules; one member of a hydrophobic interactive pair; enzyme cofactors; enzymes; polymeric acids; polymeric bases; dyes; protein binders; peptides; protein binders; and enzyme inhibitors, provided that the first and second selectable tags are different.

14. (Previously Presented) The method of claim 1, wherein the first selectable tag comprises a biotin.

15. (Previously Presented). The method of claim 1, wherein the second selectable tag comprises a biotin.

16. (Previously Presented). The method of claim 1, wherein the first selectable tag comprises a polynucleotide.

17. (Previously Presented) The method of claim 1, wherein the second selectable tag comprises a polynucleotide.

18. (Previously Presented) The method of claim 16, wherein the polynucleotide comprises, a restriction enzyme target site.

19. (Previously Presented) The method of claim 17, wherein the polynucleotide comprises a restriction enzyme target site.

20. (Currently Amended) The method of claim 1, wherein:

~~1)~~ i) the first selectable tag comprises ~~an oligonucleotide~~ a pair of oligonucleotides having a longer strand and a shorter strand, wherein each ~~with~~ strand has a 5'

end, ~~that~~ and wherein when annealed the pair of olignucleotides form a six base pair double-stranded region and an 11 base 5' single-stranded overhang, and wherein a biotin molecule is attached to the 5' end of the longer oligonucleotide strand and the 5' end of shorter oligonucleotide strand is phosphorylated at the 5' end, and wherein the 11 base 5' overhang comprises a six base nucleotide sequence which, when annealed with a single-stranded oligonucleotide comprising the complementary sequence, forms a Sma I restriction site; and

~~2)~~ii) the second selectable tag comprises ~~an oligonucleotide~~ a pair of olignucleotides having a longer strand and a shorter strand, wherein each ~~with~~ strand has a 5' end, ~~that~~ and wherein when the pair of olignucleotides annealed form a six base pair double-stranded region and an 21 base 5' single-stranded overhang, and wherein the 5' end of shorter oligonucleotide strand is phosphorylated at the 5' end, and wherein the 21 base 5' overhang comprises a six base nucleotide sequence which, when annealed with a single-stranded oligonucleotide comprising a complementary sequence, forms a Pml I restriction site.

21. (Currently Amended) The method of claim 1, wherein in step ~~(3)~~(c) the cDNA molecules in the first and second cDNA populations are denatured separately, mixed, and annealed to obtain the mixed population of cDNA molecules.

22. (Currently Amended) The method of claim 1, wherein in step ~~(3)~~(c) the cDNA molecules in the first and second cDNA populations are mixed together, denatured, and annealed to obtain the mixed population of cDNA molecules.

23. (Previously Presented) The method of claim 1, wherein an excess of cDNA from one cDNA population relative to the other is used to obtain the mixed population of cDNA molecules.

24. (Previously Presented). The method of claim 2, wherein an excess of cDNA molecules from the first cDNA population relative to cDNA molecules from the second cDNA population is used to obtain the mixed population of cDNA molecules.

25. (Previously Presented) The method of claim 24, wherein a 20-fold excess of cDNA from the first cDNA population relative to cDNA molecules from the second cDNA population is used to obtain the mixed population of cDNA molecules.

26. (Currently Amended) The method of claim 1, wherein step ~~(4)~~(d) comprises:

(i) selecting molecules comprising the first selectable tag from the mixed population to obtain a first selected population; and

(ii) selecting molecules comprising the second selectable tag from the first selected population to obtain a second selected population,

wherein the second selected population comprises the mixed population double-stranded cDNA comprising a cDNA molecule from the first cDNA population and a cDNA molecule from the second cDNA population.

27. (Currently Amended) The method of claim 1, wherein step ~~(4)~~(d) comprises:

(i) selecting molecules comprising the second selectable tag from the mixed population to obtain a first selected population; and

(ii) selecting molecules comprising the first selectable tag from the first selected population to obtain a second selected population, wherein the second selected population comprises double- stranded cDNA comprising the first and second selectable tags, and also comprises a cDNA molecule from the first cDNA population and a cDNA molecule from the second cDNA population.

28. (Currently Amended) The method of claim 1, wherein step ~~(4)~~(d) comprises contacting the mixed population with an affinity medium.

29. (Previously Presented). The method of claim 28, wherein the affinity medium comprises a compound selected from the group consisting of : biotin ; avidin; streptavidin; antigens; haptens; antibodies; hormones; vitamins; receptors; carbohydrates; lectins; metals; chelators; polynucleotides; cofactor or prosthetic groups; apoproteins; effector molecules; one member of a hydrophobic interactive pair; enzyme cofactors; enzymes; polymeric acids; polymeric bases; dyes; protein binders; peptides; protein binders; and enzyme inhibitors.

30. (Previously Presented) The method of claim 28, wherein the affinity medium comprises an affinity column.

31. (Previously Presented) The method of claim 28, wherein the affinity media comprises a solid carrier.

32. (Previously Presented) The method of claim 31, wherein the solid carrier is selected from the group consisting of: cellulose and cellulose derivatives; polyacrylamide; polystyrenes; polysaccharides; rubber; glass; nylon; polyacrylate; polyvinyltoluene; styrenebutadiamine copolymers; polyacrolein; polyurethane; poly (methyl methacrylate); and combinations thereof.

33. (Previously Presented) The method of claim 28, wherein the affinity medium comprises a magnetic particle.

34. (Currently Amended) The method of claim 1, wherein step ~~(5)~~(e) comprises contacting the double-stranded cDNA from step ~~(4)~~(d) with a reagent which binds regions of single-stranded DNA.

35. (Previously Presented) The method of claim 34, wherein the reagent which binds to regions of single-stranded DNA is selected from the group consisting of a resin which binds single stranded DNA, *E. coli* single-stranded binding protein; antibodies which bind to single-stranded DNA; and enzymes which bind to single-stranded DNA.

36. (Previously Presented) The method of claim 34, wherein the reagent which binds regions of single-stranded DNA is contained in an affinity column.

37. (Currently Amended) The method of claim 1, wherein step ~~(3)~~(c) comprises covalently linking both strands of each double-stranded cDNA from step ~~(5)~~(e) to each other to obtain a coupled molecule.

38. (Currently Amended) The method of claim 37, wherein both strands of each double-stranded cDNA from step ~~(5)~~(c) are covalently linked to each other with a polynucleotide linking moiety.

39. (Previously Presented) The method of claim 38, wherein the polynucleotide linking moiety comprises SEQ ID NO: 5.

40.-(Currently Amended) The method of claim 1, wherein step ~~(7)~~(h) comprises determining at least a partial nucleotide sequence for each strand of the coupled molecule.

41-44. (Canceled)